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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/770,943	RAZ ET AL.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 12-8-03 & 2-25-04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-9, 11-14, 22, 23 & 25-29 is/are pending in the application.

4a) Of the above claim(s) 6-9 - 14, 22, 23 & 25-29 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-5 & 11-13 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-9, 11-14, 22, 23 & 25-29 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response to the restriction requirement and amendment filed 12/8/03 have been entered into the record. The response to the informal amendment filed 2-25-04 has been entered into the record. Claims 1-9, 11-14, 22, 23 and 25-29 are pending. Claims 10, 15-21 and 24 having been canceled.

Priority

Applicants are requested to update the status of all nonprovisional parent application referenced in the claim for benefit under 35 U.S.C. 120.

Information Disclosure Statement

The information disclosure statement filed 1-26-02 has been considered. A initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group I, in the response of 12-8-03 is acknowledged. The traversal is on the ground(s) that no restriction was required in the Parent and that the claims of at least Groups I-XII, XXIV, XXVI and XXVII should therefore be examined together because they were examined together in the Parent. This is not persuasive. The lack of a restriction in the parent does not obviate the restriction between non-allowable products and corresponding methods of use. Further, claims 6-9 are not commensurate with the allowed composition claims. The methods of the elected invention will be rejoined when the elected composition products become allowable, provided that Applicants maintain a corresponding scope.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-9, 14, 22, 23 and 25-29 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions. Applicant timely traversed the restriction (election) requirement in the response of 12-8-03.

Claim Objections

Claims 11-13 are objected to because of the following informalities: The claims depend in the alternative from non-elected subject matter. Appropriate correction is required.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 1-5 and 10 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-5 and 11 of prior U.S. Patent No. 6,255,292. This is a double patenting rejection. The claimed compositions are structurally identical. The recitation of the preamble is not given patentable weight because it does not limit the composition *per se* and merely provides for intended use of the claimed composition.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 12 recites a kit for use in gene therapy or gene immunization consisting of the immunoinhibitory nucleic acid of the elected invention in a sterile vial and an recombinant expression vector in a sterile vial and claim 13 provides for the combination in the same sterile vial. The specification is devoid of any data related to the ability to immunoinihibit an immune response to a gene therapy antigen or gene immunization antigen.

The specification teaches that the claimed immunoinhibitory nucleic acid having the claimed hexamer structure provides for decrease in Th1 type immune response (Figure 4) and an increase in Th2 type immune response to antigens (page 18, first full paragraph and Figure 5). The specification and art teaches that Th1 type immune responses provide for an increase in IgG2a while a Th2 type immune response provides for an increase in IgG1 and IgE (page 9, first full paragraph and page 10, paragraph d.) indicating that only the

Th1 type immune response of the immune stimulatory nucleotide sequence is subject to inhibition by the immunoinhibitory nucleic acid. The Th2 type immune response is promoted by the claimed immunoinhibitory nucleic acids resulting in an immediate type hypersensitivity antibody (IgE) which mediates allergic disease. As such, the immunoinhibitory nucleic acid hexamer is very specific for the Th1-type immune response and is not "immunosuppressive" in that antigen specific antibody is still produced, but the isotype is altered. The specification fails to teach that the immunoinhibitory nucleic acid results in suppression of the immune response to recombinant expression vector antigens. The specification alledges that control of the Th1/Th2 mediated cytokine release enables one to control host immune response to recombinant vector antigens having clinical significance for control of gene expression for gene therapy and gene immunization (page 22, lines 10-15). The specification lacks any data indicating that the claimed nucleic acids suppress the endogenous immune response to vector antigens as alleged. Furhter, the specification specifically teaches that the inhibitory nucleic acids promote IgG1 and IgE antibody production. As such, the immunoglobulin isotype switch would not be of clinical significance for control of gene expression for gene therapy and gene immunization because an antibody response is still produced. The art teaches that immunostimulatory DNA sequences are at least necessary for effective intradermal gene immunization (Sato et al , Science Bol 273, 1996; reference CK of record). As such, the immunostimulatory sequences appear necessary for effective gene immunization. Immunization is defined in the art as (1) adminstration of an antigen in order to produce an immune response to that antigen or (2) in clinical contexts the term is used more specifically to mean administration of ether antigen to produce active immunity or antibody to produce passive immunity, in order to confer protection against harmful effects of antigenic substances or organisms (see Herbert et al., The Dictionary of Immunology, Fourth Edition, Academic Press Inc, San Diego CA, 1995 page 89). The alleged clinical significance of promoting IgG2 and IgE responses in an individual undergoing gene immunization presumably toward an antigen is

not provided for by the specification and the specification fails to teach any antigen for which IgE immunization provides for a protective response. Further, the specification fails to teach that such immunization generates a protective immune response in the clinical sense toward the desired antigen. Tripathy et al (Nature Medicine 2(5):545-50, 1996) teaches that immune responses to transgene-encoded "non-self" proteins limit the stability of gene expression after injection of replication-defective adenovirus vectors and that this is important for the design of further preclinical and clinical gene therapy trials. Tripathy et al also teach that both a cellular and humoral immune response are responsible for the elimination of gene expression in adenovirus mediated gene therapy. With respect to gene therapy, this therapy is in general is to replace absent or non-functioning genes. In any animal with the gene abscent or non-functioning, the transgene would be seen as "non-self" in the targeted population for gene therapy. The specification is devoid of data indicating that the cellular and humoral immune responses toward any gene therapy protein is suppressed allowing for long term recombinant gene expression in any relevant animal model. The specification teaches that the claimed immunoinhibitory nucleic acids provide for a Th2-type response resulting in the production of IgE (see figure 5). As such, the specification fails to teach that the claimed immunoinhibitory nucleic acids provide for lack of response to the transgene. In fact, the specification would appear to teach that the response would be directed toward an IgG2 and IgE response rather than an IgG1 response. IgG2 and IgE also bind antigen and as such, it is unclear as to how the generation of different antibody isotypes provides for long term recombinant gene expression when antigen-specific antibody is still produced. Additionally, the specification does not address the issue of ongoing expression of the transgene and how this affects the IgG2 and IgE response. Applicants' specification indicates that while the administration of the claimed immunoinhibitory nucleic acids may inhibit Th1 type antibody responses (Figure 4), they promote Th2 type antibody responses (see Figure 5) when administered with antigen and later boosted (Figure 5). The

generation of Th2-type antibody response is also a clinically deleterious immune response (i.e. hypersensitivity IgE) and the antibodies produced would necessarily bind the non-self transgene. The specification fails to take into account the complicated situation of long-term recombinant gene expression and how this affects the ongoing immune response in an immunocompetent host. The specification fails to address the generation of the CD8+ T cell response which has also been demonstrated to be involved in the transient expression of the transgene (see Tripathy, page 545, column 1, second full paragraph). The specification fails to teach that the administration of any gene for therapy or gene for immunization provides for a suppression of the CD8+ immune response and as such would necessarily result in the clinical benefit of the lack of an this immune response to the nucleic acid expressed antigen or transgene. There is no data in this specification indicating the suppression of the immune response in general to an antigen, but merely shifting to a Th2 type immune response (Figure 5). There is no data indicating that the claimed immunoinhibitory nucleic acids provide for suppression of the immune response to any gene immunization antigen. In fact, the specification teaches that IgE is generated in response to administering the immunoinhibitory nucleic acid with antigen. The specification is devoid of any data addressing the ability of the claimed immunoinhibitory nucleic acid sequences for suppression of immune responses for use in gene therapy or gene immunization as asserted in the specification. Additionally, the specification fails to take into account the complicated and unpredictable nature of gene therapy and gene immunization as evidenced by the art of record. The ability to provide for gene therapy is highly unpredictable and the specification fails to teach successful gene therapy or gene immunization using any antigen in combination with the claimed immunoinhibitory nucleic acid sequences as claimed.

In the absence of further guidance from Applicants because of the lack of any data in the specification directed to gene immunization or gene therapy, the demonstration of a Th2 type antibody response to antigen and when co-adminstered with the immunoinhibitory

nucleic acid sequence, the highly unpredictable nature of gene therapy and gene immunization, it would require undue experimentation to use the recombinant expression vector and immunoinhibitory nucleic acid sequence for gene therapy or gene immunization as claimed.

Claim 12 and 13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to a kit for use in gene immunization using an immunoinhibitory compound. This is inherently contradictory, if a compound is immunoinhibitory then immunization can not take place because immunization requires an immune response. Further, the claims do not positively recite a gene for therapy or immunization and as such, it is completely unclear how the kit can be used for either gene thereapy or gene immunization when there is no gene of interest present.

Status of the Claims

Claims 1-5 and 11-13 stand rejected.

Conclusion

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-F 6:30 pm - 3:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patricia A. Duffy, Ph.D.

Primary Examiner

Art Unit 1645